FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Meeting of the Psychopharmacologic Drugs Advisory Committee (PDAC)
FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503)
10903 New Hampshire Avenue, Silver Spring, Maryland
December 1, 2015

DRAFT QUESTIONS

The Food Drug and Cosmetic Act requires a sponsor to provide substantial evidence of effectiveness to support approval of a new drug. The Act defines the level of evidence necessary as generally requiring two positive adequate and well-controlled trials.

1. **DISCUSSION:** Please discuss the following questions related to substantial evidence:

    a. In the situation where two positive adequate and well-controlled trials have been completed, how much and what type of "negative evidence" from other negative or failed trials would it take to undermine a finding of substantial evidence of effectiveness?

    b. What approaches for synthesizing evidence across positive and negative/failed trials in a development program are useful for decision-making?

2. **DISCUSSION:** Please discuss your views on ways to evaluate clinical trials for assay sensitivity. Please consider the following questions in your discussion:

    a. Is the primary endpoint for efficacy prospectively defined in the protocol the only meaningful way to evaluate assay sensitivity?

    b. Can *post hoc* analyses of other efficacy endpoints or use of other analysis methods contribute to the determination of assay sensitivity?

3. **VOTE:** Has the sponsor provided substantial evidence of effectiveness for gepirone extended-release (ER) in the treatment of major depressive disorder (MDD)?

4. **VOTE:** Has the sponsor adequately characterized the safety profile of gepirone ER in the treatment of MDD?

5. **VOTE:** Do the available data support a favorable benefit risk profile of gepirone ER to support approval?

6. **DISCUSSION:** What, if any, additional studies are needed pre- or post-approval to address outstanding issues, e.g., an additional effectiveness study, an additional randomized withdrawal maintenance trial?